DWIST

[Duloxetine]

20mg, 30mg & 60mg Capsules

ڈوِسٹ

۲۰ ملی گرام، ۳۰ ملی گرام اور ۶۰ ملی گرام کیپسولز

QUALITATIVE AND QUANTITATIVE COMPOSITION:

DWIST (Duloxetine) is available for oral administration as:

1.**DWIST** Capsules 20mg
Each capsule contains:
Duloxetine Hydrochloride enteric coated pellets equivalent to Duloxetine.....20mg
(Product Specs.: USP)

2.**DWIST** Capsules 30mg
Each capsule contains:
Duloxetine Hydrochloride enteric coated pellets equivalent to Duloxetine.....30mg
(Product Specs.: USP)

3.**DWIST** Capsules 60mg
Each capsule contains:
Duloxetine Hydrochloride enteric coated pellets equivalent to Duloxetine.....60mg
(Product Specs.: USP)

CLINICAL PHARMACOLOGY:

MECHANISM OF ACTION:

Duloxetine is a combined serotonin (5-HT) and noradrenaline (NA) reuptake inhibitor. It weakly inhibits dopamine reuptake, with no significant affinity for histaminergic, dopaminergic, cholinergic, and adrenergic receptors. Duloxetine dose-dependently increases extracellular levels of serotonin and noradrenaline in various brain areas. Duloxetine normalizes pain thresholds of neuropathic and inflammatory pain and attenuated pain behaviour in a model of persistent pain. The pain inhibitory action of duloxetine is believed to be a result of potentiation of descending inhibitory pain pathways within-the central nervous system.

PHARMACOKINETICS:

Absorption:

Orally administered duloxetine hydrochloride is well absorbed. Maximal plasma concentrations (C_{max}) of duloxetine occurs within 6 hours post dose. Food does not affect the maximal plasma concentrations (C_{max}) of duloxetine but delays the time to reach peak concentration from 6 to 10 hours and it marginally decreases the extent of absorption (AUC) by about 10%. There is a 3 hour delay in absorption and a one-third increase in apparent clearance of duloxetine after an evening dose as compared to a morning dose.

Distribution:

Duloxetine is approximately 96% bound to human plasma proteins. Duloxetine binds to both albumin and α_1-acid glycoprotein. Protein binding is not affected by renal or hepatic insufficiency.

Metabolism:

Duloxetine is extensively metabolized by CYP P450-2D6 and 1A2 to a pharmacologically inactive metabolites.

Excretion:

The elimination half-life ($t_{1/2}$) of duloxetine ranges from 8 to 17 hours. Metabolites are principally excreted in the urine; about 20% is excreted in the feces.

THERAPEUTIC INDICATIONS WITH DOSAGE & ADMINISTRATION:

DWIST (Duloxetine) should be swallowed whole and should not be chewed or crushed, nor should the capsule be opened and its contents sprinkled on food or mixed with liquids. **DWIST** should be given without regard to meals.

No.	INDICATION	STARTING DOSE	TARGETED DOSE	MAXIMUM DOSE
1)	**Major Depressive Disorder**	* 30mg/day for first week	**Acute Treatment:** 20mg or 30mg twice daily to 60mg once daily **Maintenance Treatment:** 60mg/day	120mg/day
2)	**Generalized Anxiety Disorder**	* 30mg/day for first week	**60mg once daily or 30 mg twice daily**	120mg/day
3)	**Diabetic Peripheral Neuropathic Pain**	60mg/day	**60mg once daily or 30 mg twice daily**	60mg/day
4)	**Fibromyalgia**	* 30mg/day for first week	**60mg once daily or 30 mg twice daily**	60mg/day
5)	**Chronic Musculoskeletal Pain**	* 30mg/day for first week	**60mg once daily or 30 mg twice daily**	60mg/day

* Dosing may be started at 30 mg for one week, to allow patients to adjust to the medication before increasing to 60 mg once daily.
Some patients may benefit from starting at 30mg once daily.
There is no evidence that doses greater than 60mg/day confers additional benefit, while some adverse reactions were observed to be dose-dependent.

Special Population:

Renal Impairment:

DWIST is not recommended for patients with end-stage renal disease or severe renal impairment (estimated creatinine clearance < 30mL/min).

Hepatic Impairment:

Caution should be exercised in hepatic impairment.

Elderly:

Caution should be exercised when treating the elderly.

Discontinuation of Treatment:

Abrupt discontinuation should be avoided. When stopping treatment with **DWIST** the dose should be gradually reduced over a period of at least 1 to 2 weeks in order to reduce the risk of withdrawal reactions. If intolerable symptoms occur following a decrease in the dose or upon discontinuation of treatment, then resuming the previously prescribed dose may be considered. Subsequently, the physician may continue decreasing the dose, but at a more gradual rate.

CONTRAINDICATIONS:

Duloxetine is contraindicated in patients:

- With hypersensitivity to the active substance or to any of the excipients.
- Taking monoamine oxidase inhibitors (MAOIs).
- Taking with fluvoxamine, ciprofloxacin or enoxacine (i.e., potent CYP1A2 inhibitors).
- With severe renal insufficiency with creatinine clearance < 30mL/min.
- In patients with uncontrolled hypertension.

PRECAUTIONS:

WARNING: SUICIDALITY AND ANTIDEPRESSANT DRUGS: Antidepressants increased the risk of suicidal thoughts and behavior in children, adolescents, and young adults in short-term studies. These studies did not show an increase in the risk of suicidal thoughts and behavior with antidepressant use in patients over age 24; there was a reduction in risk with antidepressant use in patients aged 65 and older. In patients of all ages who are started on antidepressant therapy, monitor closely for worsening, and for emergence of suicidal thoughts and behaviors. Advise families and caregivers of the need for close observation and communication with the prescriber

Use **DWIST** with caution in;

- Patients with a history of mania or a diagnosis of bipolar disorder and/or seizures.
- Patients with increased intra-ocular pressure or those at risk of acute narrow-angle glaucoma.
- Cardiovascular compromised patients with increased heart rate or increase in blood pressure, continuous blood pressure monitoring is recommended.
- Patients taking anticoagulants or antiplatelet and in patients with known bleeding tendencies to avoid hemorrhage.
- Patients at increased risk for hyponatremia; such as elderly, cirrhotic, or dehydrated patients, or patients treated with diuretics.
- Patients treated with other medicinal products associated with hepatic injury as severe elevations of liver enzymes, hepatitis and jaundice may occur with duloxetine.-
- Patient using **DWIST** sedation & dizziness may occur, avoided driving and using machinery.
- Children & adolescent below the age of 18 years.
  Discontinued **DWIST**;
- First appearance of sign of hypersensitivity
- For patients who experience a sustained increase in blood pressure while receiving dulo-
- Xetine, either dose reduction or gradual discontinuation should be considered.

Pregnancy:

Duloxetine should be used in pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers:

Contraindicated during lactation.

DRUG INTERACTIONS:

Monoamine Oxidase Inhibitors (MAOIs): Due to the risk of serotonin syndrome, duloxetine should not be used in combination with non-selective irreversible monoamine oxidase inhibitors , or within at least 14 days of discontinuing treatment with an MAOI. Based on the half-life of duloxetine, at least 5 days should be allowed after stopping Duloxetine before starting an MAOI.

CNS Drugs: Caution is advised when **DWIST** is taken in combination with centrally acting drugs or substances, including alcohol and sedative medicinal products (e.g. benzodiazepines, morphinomimetics, antipsychotics, phenobarbital, sedative antihistamines).

Serotonergic Agents: Caution is advisable if **DWIST** is used concomitantly with serotonergic agents like clomipramine, amitriptyline, moclobemide, linezolid, St John's wort (Hypericum perforatum), triptans, tramadol pethidine and tryptophan to avoid serotonin syndrome.

Drugs Metabolised by CYP2D6:

Caution is advised if **DWIST** is co-administered with drugs that are metabolised by CYP2D6 and particularly if they have a narrow therapeutic index.

Anticoagulants and Antiplatelet Agents: Use with caution concomitantly with NSAIDs, aspirin, warfarin to avoid bleeding disorders.

ADVERSE REACTIONS:

Very Common: Nausea, headache, insomnia, fatigue, somnolence, dry mouth, dizziness and constipation.In patients with diabetic neuropathic pain, it was seen during the clinical trials **DWSIT** had an elevation in fasting blood glucose levels.

Common: Gastrointestinal disturbances, anxiety, visual disturbances, weight gain or loss, sexual dysfunction, lethargy, increased sweating and pruritus. Dose-related increases in bloodpressure also occurs in some patients.

OVERDOSAGE: Signs and symptoms of overdose include somnolence, coma, serotonin syndrome, seizures, syncope, tachycardia, hypotension, hypertension and vomiting.No specific antidote is known for duloxetine but if serotonin syndrome occurs, treatment with cyproheptadine may be considered. A free airway should be established. Monitoring of cardiac and vital signs is recommended,along with appropriate symptomatic and supportive measures. Gastric lavage may be indicated if performed soon after ingestion or in symptomatic patients. Activated charcoal may be useful in limiting absorption.

INSTRUCTIONS:
- Store below 30°C
- Protect from light & moisture
- Keep out of reach of children

To be sold on prescription of a registered medical practitioner.

HOW SUPPLIED:

DWIST (Duloxetine) Capsules 20mg are available in packs of 14's.
DWIST (Duloxetine) Capsules 30mg are available in packs of 10's.
DWIST (Duloxetine) Capsules 60mg are available in packs of 10's.

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
ہدایت: دوا کو ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
روشنی اور نمی سے بچائے۔ بچوں کی پہنچ سے دور رکھیں۔
صرف رجسٹرڈ ڈاکٹر کے نسخے کے مطابق فروخت کریں۔

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